

Literature Review

Comparison radical surgery versus conservative surgery to decrease post-operative recurrence in ossifying fibroma: systematic review

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Abstract – Background: Ossifying fibroma in craniofacial is a rare disease, benign, locally aggressive fibro-osseous tumor. In the recent 2017 WHO classifications, ossifying fibroma divided into 2 type, ossifying fibroma of odontogenic origin and juvenile ossifying fibroma. Choosing the right treatment that can reduce the recurrence rate are particularly challenging. In this systematic review we try to analyse related study to determine the best treatment for ossifying fibroma. **Aim:** The aim of this review to evaluate best treatment option and analysed level of recurrence in each type of treatment. **Method:** Collected Juvenile Ossifying Fibroma (JOF) and Ossifying Fibroma (OF) related Article from four different database (PubMed, Scopus, Cochrane Library, and Proquest). Study selection was done by using PRISMA strategy. **Result:** Eight retrospective case series studies were analyzed. Recurrence rate after surgery was 15.3%, most frequent recurrence occurs in conservative surgery. Recurrence rate after conservative surgery was 19.7%, compared with radical surgery which relatively lower in percentage, with recurrence rate after surgery was 10.6%. **Conclusion:** Juvenile Ossifying Fibroma, especially Trabecular Juvenile Ossifying Fibroma (TrJOF), show high recurrence percentage comparing other type. The first-choice management for treating OF was surgical approach. Types of surgery choose to depend on the aggressiveness and morbidity of the disease. Radical surgery was proven better to decrease level of recurrence compared with conservative surgery.

Introduction

Fibro-osseous lesion is benign tumour characterized by the replacement of normal bone by a fibrous cellular stroma containing various amounts of foci of mineralisation or ossification [1]. Waldron stated the lesion usually describe as pathological changes within the jaw bones, in which normal bone is replaced by fibrous tissue with or without calcification. They frequently develop in the craniofacial region, especially in the jaws, the nasal cavity, the paranasal sinuses and the orbit [2]. They are divided into 3 different entities, namely osteoma, fibrous dysplasia (FD) and ossifying fibroma (OF). Osteoma is the most frequent subtype, followed by FD and OF [1].

OF is a benign fibro-osseous lesion that arises in the head and neck region. The lesion can occur at any age and in both sexes, but it has been reported to most frequently occur in young adulthood with a female predominance [3]. In 2005, ossifying fibroma was included under the bone-related lesions in the WHO classification of odontogenic tumours. ossifying

fibroma divided into 2 type, ossifying fibroma of odontogenic origin and juvenile ossifying fibroma. Juvenile ossifying fibroma (JOF) is a variant of ossifying fibroma and described as a benign neoplasm commonly affecting the extra-gnathic craniofacial skeleton of the young individuals. The Psammomatoid Juvenile Ossifying Fibroma (PsJOF) and Trabecular Juvenile Ossifying Fibroma (TrJOF) variants are the subtypes of JOF. PsJOF and TrJOF are distinct in clinico-pathologic entities, affecting different age groups, site predilection, and with distinguishing histopathological features. PsJOF is observed in a wider age range and predominantly found in the sinonasal and orbital bones, whereas TrJOF affects patients of a younger age group, more aggressive and mainly affects the jaws [4].

The treatment of JOF, generally based on histological subtype and tumour aggressiveness, is highly individualized. A conservative approach is indicated in some cases, and a more radical approach including a surgical resection may be needed in other cases. Choosing the right treatment that can reduce the recurrence rate are particularly challenging. This systematic review tried to analyse related study to determine the best treatment with low recurrence level for ossifying fibroma.

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Objective

The high rate of recurrence level in OF still reported by several study that conducted in recent years. Surgical treatment selection in initial management become important factor that influence recurrence rate. Surgical treatment in OF cases divided in 2 type, conservative surgery, including enucleation and curettage, and radical surgery, including local, marginal, and total resection. The aim of this review to evaluate best treatment option and analysed level of recurrence in each type of treatment.

Method

Search strategy

Parameters used for identifying studies that were initially considered for this systematic review is to analyze the effectiveness of surgical treatment effective to manage and decrease recurrence of ossifying fibroma.

- P: Patient with Ossifying fibroma
- I: Radical Surgery
- C: Conservative surgery
- O: to manage and decrease recurrence

Data Sources and search terms

A comprehensive electronic literature search was performed on March 2nd, 2020 using four different online databases (PubMed, Scopus, Cochrane Library, and Proquest). Article search also done by searching the bibliography from previous article. The Boolean search terms in this systematic review were described below:

- (Ossifying Fibroma OR Fibro-osseus lesion) AND
- Craniofacial AND
- Surgical treatment

Limits placed on the literature search included humans, English language, Randomized controlled trial (RCT), Cohort, Case control, Cross sectional and case series in the last ten years (2010 to 2020). All articles were screened and examined from the titles and abstracts, and potentially relevant studies were reviewed in full articles.

Inclusion and exclusion criteria

Inclusion Criteria:

- Study in human
- Study related Juvenile Ossifying fibroma OR Ossifying fibroma.
- The study took the form of Randomized controlled trial (RCT), Cohort, Case control, and Cross sectional.
- Study analyses include comparing between radical surgery and conservative surgery, recurrence level between those procedures.

Exclusion criteria:

- Article not in English
- Not full text article

Data extraction

The following information was extracted from all studies included: (1) demographic characteristics of participant, (2) Type of Ossifying fibroma, (3) Type of surgery, (4) Duration of follow up, (5) recurrence rate in each type of surgery, (6) average time of recurrence.

Quality assessment

Critical appraisal had been done by writer, using critical appraisal method based on critical appraisal for treatment study available at www.cebm.net. After assessed the Article, authors reported the result of critical appraisal through [Table I](#), that is explaining about validity, importance, and applicability based on content of each article.

Result

Search finding

A literature search was conducted through Article databases using keywords "Ossifying fibroma" AND "Craniofacial" AND "Surgical management" AND "Recurrence".

Process of studies selection was done by two reviewers. Records identified through 4 databases searching (PubMed, Cochrane, Proquest, and Scopus) resulted 82 articles. Record after duplicates removed was 52 articles. After titles and abstract screening resulted 16 articles. Full text assessed based on eligibility criteria (inclusion criteria and exclusion criteria) found 8 articles. At the end, authors analysed 8 retrospective case series studies for qualitative synthesis. The selection strategy was summarized in [Figure 1](#).

Quality of included studies

The methodological quality of studies were assessed using critical appraisal method based on critical appraisal for treatment study available at www.cebm.net. The quality assessment result presented through [Table I](#).

Risk assessment of Bias

We used the tool from Risk of Bias Assesment for Case-Series using Joanna Brigg's Critical Appraisal Tool for Case-Series. The plus (+) sign represent answer "Yes" (low risk of bias), whereas the minus (-) sign represent answer "No" (high risk of bias), N/A mean not applicable and "Unclear" sign indicate that it was not clearly stated in the study. If answer "Yes" showed in 5-10 question, the overall appraisal was low risk of bias. If answer "Yes" showed 1-4, the overall appraisal was high risk of bias ([Table II](#)).

Characteristic of included studies

Demographic characteristics of the sample

Demographic characteristics of the study populations such as the ratio of male and female and age were described by all studies ([Table III](#)). Type of OF based on WHO classification also

Table I. Critical appraisal based on VJA.

Article	Study Design	Sample	Validity			Importancy		Applicability			Levels of evidence*		
			Randomization	Similar	Treated equally	Intention to Treat	Blinding	Result	Precision	Similarity		Feasibility	Potential benefit
Liu Y <i>et al.</i> (2010) [5]	Case series	20	-	-	-	-	-	N/A	-	+	+	+	4
Suarez-Soto (2013) [6]	Case series	19	-	-	-	-	-	N/A	-	+	+	+	4
Mohanty <i>et al.</i> (2014) [7]	Case series	25	-	-	-	-	-	N/A	-	+	+	+	4
Han <i>et al.</i> (2015) [8]	Case series	63	-	-	-	-	-	N/A	-	+	+	+	4
Kumar <i>et al.</i> (2015) [9]	Case series	10	-	-	-	-	-	N/A	-	+	+	+	4
Titinchi <i>et al.</i> (2016) [10]	Case series	61	-	-	-	-	-	N/A	-	+	+	+	4
Liu Y <i>et al.</i> (2017) [11]	Case series	42	-	-	-	-	-	<0.001	-	+	+	+	4
Liu JJ (2017) [12]	Case Series	13	-	-	-	-	-	N/A	-	+	+	+	4

* Levels of evidence based on center of evidence medicine University of Oxford 2011.

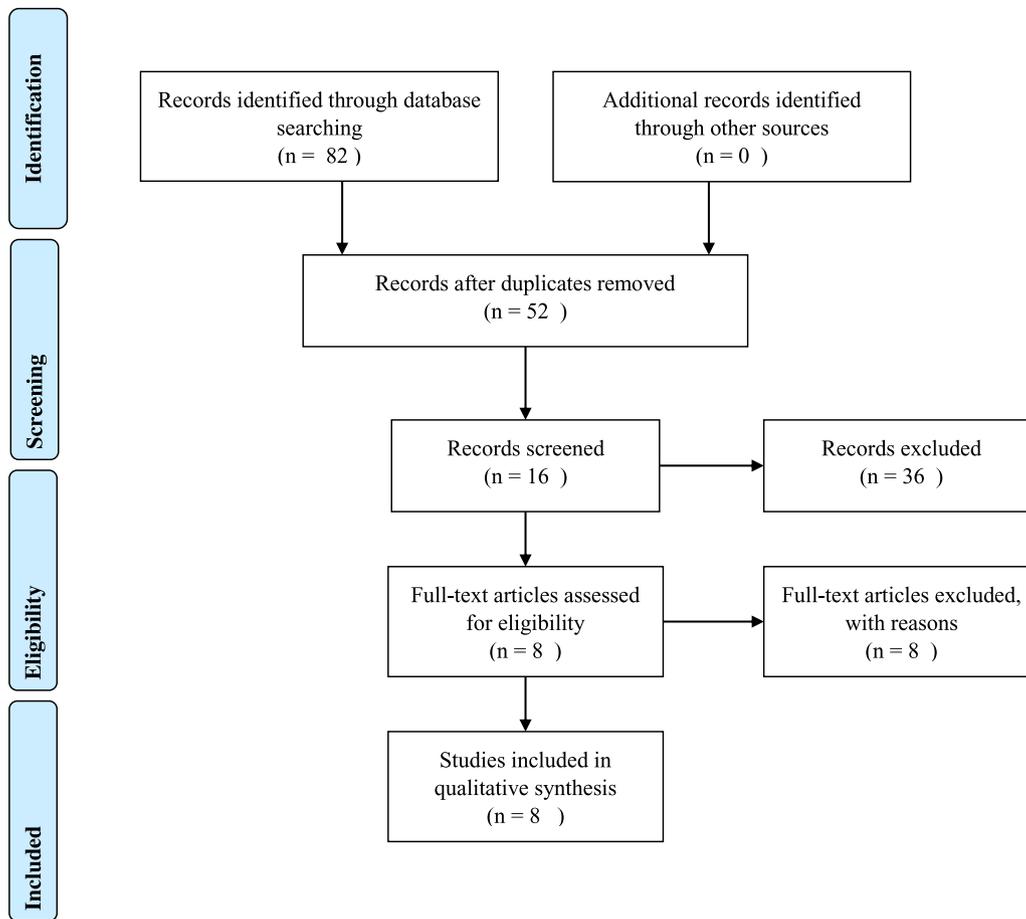


Fig. 1. Prisma chart.

stated by all studies. Most of studies were case series study with small sample size study, there are 2 studies that had more than 50 sample size. Total sample from 8 case series studies was 213 patients. Global prevalence from included study showed more frequent in female than male with percentage 55.4% and 44.6% respectively. Male to female ratio was 1:1.2. Predominant group of age was below 18 years old with total percentage 51.6%, in group of age above 18 years old was 40.8%.

Type of Ossifying fibroma

In 2005, ossifying fibroma was included under the bone-related lesions in the WHO classification of odontogenic tumours. In the recent 2017 WHO classifications, classifications of OF divide into (1) Ossifying fibroma of odontogenic origin (cemento-ossifying fibroma) and (2) Juvenile ossifying fibroma (JOF), which is further divided into two distinct types: Trabecular Juvenile Ossifying fibroma (TrJOF) and Psammomatoid Juvenile Ossifying fibroma PsJOF). Based on the 8 studies included in this review, the frequent prevalence is OF (71.4%) followed by JOF (25.4%). For the JOF subtype, most studies report the incidence of TrJOF more often than PsJOF with a percentage prevalence of 10.3% and 8.9%, respectively. Most frequent site of predilection was mandible with percentage 55.9 % followed with maxilla 30.9%, only 1 study

reported predilection in paranasal sinus with total percentage 3.6%. Radiological findings from most included studies reported the pathognomonic sign of OF in radiology was well-defined margin with percentage of cases 62.9%, follow with ill-defined margin 12.2%, and moderate-defined margin 0.9%.

Type of surgery

Type of surgery reported in included study divided into 2 types, conservative surgery and radical surgery. Conservative surgical procedure including curettage, enucleation or peripheral osteotomies. Radical surgery including local resection, marginal resection and total resection with or without reconstructive surgery. Most of studies implemented 2 type of surgery (radical and conservative surgery) in their patient, only 1 study (Kumar *et al.* [9]) reported using radical surgery to treat all their patients. Radical surgery was the most preferable treatment that chosen by surgeon based on this review with percentage 35.7% compared with conservative surgery with percentage 28.6%.

Recurrence rate after surgery

Recurrence rate after surgery reported vary between studies. Global recurrence rate after surgery was 14.4% with most frequent recurrence occurs in conservative surgery. Recurrence

Table II. Risk of bias assessment for case-series using Joanna Brigg’s critical appraisal tool for case-series.

	Were there clear criteria for inclusion in the case series?	Was the condition measured in a standard, reliable way for all participants included in the case series?	Were valid methods used for identification of the condition for all participants included in the case series?	Did the case series have consecutive inclusion of participants?	Did the case series have complete inclusion of participants?	Was there clear reporting of the demographics of the participants in the study?	Was there clear reporting of clinical information of the participants?	Were the outcomes or follow up results of cases clearly reported?	Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	Was statistical analysis appropriate?	Overall Appraisal
Liu Y et al. (2010) [5]		Unclear	Unclear							N/A	High Risk
Suarez-Soto et al. (2013) [6]						Unclear	Unclear	Unclear		N/A	Low Risk
Mohanty et al. (2014) [7]										N/A	Low Risk
Han et al. (2015) [8]											Low Risk
Kumar et al. (2015) [9]								Unclear		N/A	Low risk
Titinchi et al. (2016) [10]											Low risk
Liu Y et al. (2017) [11]											Low risk
Liu JJ et al. (2017) [12]	Unclear	Unclear			Unclear					N/A	High Risk

rate after conservative surgery was 19.7%, compared with radical surgery which relatively lower in percentage, with recurrence rate after surgery was 10.6% (Table IV).

Recurrence Time

From 8 included studies, only 2 studies reported time of recurrence, there was Liu Y *et al.* [11], and Han *et al.* [8]. The both of studies reported similar, recurrence will happen in 3–52 months (Liu Y *et al.* [11]) and 6 months to 5 years. Liu Y *et al.* [11] reported almost 75% of cases recurred in 1 years after surgery.

Discussion
Search finding

The preliminary result of the literature search for this study were 82 articles. Most of articles in the form of case series study or case report studies. Record after duplicates removed was 52 articles. After titles and abstract screening resulted 16 articles. Full text assessed based on eligibility criteria (inclusion criteria and exclusion criteria) found 8 articles. At the end, authors analysed 8 retrospective case series studies for qualitative synthesis.

Table III. Demographic characteristic of studies.

No	Author, Year	total Sample	Gender		Age	Type of Ossifying fibroma			Site of Predilection		Radiological Finding		Type of Surgery		Recurrence after surgery	Average Recurrence Time	
			Male	Female		<18 Years	>18 Years	Ossifying fibroma	Trabecular Ossifying fibroma	Psammomatoid fibroma	Mandible	Maxilla	Paranasal Sinuses	Well-Defined			Moderate III — defined
1	Liu Y <i>et al.</i> (2010) [5]	20 Patients	(9/20) 45%	(11/20) 55%	(7/20) 35%	(13/20) 65%	(20/20) 100%	N/A	(16/20) 80%	(4/20) 20%	N/A	(5/20) 25%	(1/20) 5%	(7/9) 77.8%	(2/9) 22.2%	(1/7) 14.3% (1/2) 50%	N/A
2	Suarez-Soto (2013) [6]	19 Patients	(1/3) 33.3%	(2/3) 66.7%	(2/3) 66.7%	(1/3) 33.3%	(3/19) 15.8%	N/A	(1/3) 33.3%	(2/3) 66.7%	N/A	N/A	N/A	(2/3) 66.7%	(1/3) 33.3%	0% 100%	N/A
3	Mohanty <i>et al.</i> (2014) [7]	25 patients	(14/25) 56%	(11/25) 44%	(6/25) 24%	(19/25) 76%	(24/25) 96%	N/A	(18/25) 72%	(7/25) 28%	N/A	(15/25) 60%	(2/25) 8%	(4/25) 16%	(21/25) 84%	0% 0%	N/A
4	Han <i>et al.</i> (2015) [8]	15 Patients	(5/15) 33.3%	(10/15) 66.7%	(15/15) 100%	N/A	N/A	(10/15) 66.7%	(9/15) 60%	(6/15) 40%	N/A	(13/15) 86.67%	(2/15) 13.33%	(6/15) 40%	(9/15) 60%	0% 33.3%	17.1 Months (6 Months — 5 years)
5	Kumar <i>et al.</i> (2015) [9]	10 Patients	(6/10) 60%	(4/10) 40%	(4/10) 40%	(6/10) 60%	(2/10) 20%	(4/10) 40%	(7/10) 70%	(3/10) 30%	N/A	N/A	N/A	100%	0%	0%	N/A
6	Tifinchi <i>et al.</i> (2016) [10]	61 Patients	(22/61) 36.1%	(39/61) 63.9%	(22/61) 39.3%	(39/61) 60.7%	(61/61) 100%	N/A	(41/61) 67.2%	(16/61) 26.22%	N/A	(57/61) 94%	N/A	(4/22) 18.2%	(18/22) 81.8%	(1/8) 5.5% (6/35) 17.1%	N/A
7	Liu Y <i>et al.</i> (2017) [11]	50 Patients	(34/50) 68%	(16/50) 32%	(50/50) 100%	N/A	(29/50) 58%	(12/50) 24%	(27/50) 54%	(23/50) 46%	N/A	(44/50) 88%	N/A	(35/50) 70%	(7/50) 14%	(6/7) 86%	3-52 Months 75% of cases relapse in 1 year
8	Liu JJ <i>et al.</i> (2017) [12]	13 Patients	(4/13) 31%	(9/13) 69%	(4/13) 30.8%	(9/13) 69.2%	(9/13) 69.2%	N/A	N/A	(5/13) 38.5%	N/A	N/A	N/A	(8/13) 69.2%	(3/13) 23.1%	(2/8) 25% (1/3) 33.3%	N/A
Total Percentage		200 Patients	(95/213) 44.6%	(118/213) 55.4%	(110/213) 51.6%	(87/200) 40.8%	(152/213) 71.4%	(54/213) 25.4% (22/213) 10.3%	(119/213) 55.9%	(61/200) 30.9%	(8/213) 3.6%	(134/213) 62.9%	(2/213) 0.9%	(26/200) 12.2%	(61/213) 28.6%	Radical surgery: (9/76) 11.8% Conservative surgery: (12/61) 19.7%	

*OF: Ossifying fibroma, COF: Central-Ossifying Fibroma, POF: Peripheral Ossifying Fibroma, JOF: Juvenile Ossifying Fibroma, TrJOF: Trabecular Juvenile Ossifying Fibroma, PsJOF: Psammomatoid Juvenile Ossifying Fibroma.

Table IV. Recurrence rate based on ossifying fibroma subtype.

No	Author Year	Type of Ossifying fibroma			Reccurrence rate
		Ossifying fibroma	Trabecular Ossifying fibroma	Psammomatoid Ossifying fibroma	
1	Liu Y <i>et al.</i> (2010) [5]	(20/20) 100%	N/A	N/A	(2/9) 22.2%
2	Suarez-Soto <i>et al.</i> (2013) [6]	(3/19) 15.8%	N/A	N/A	OF: (1/3) 33.3%
3	Mohanty <i>et al.</i> (2014) [7]	(24/25) 96%	N/A	(1/25) 4%	0%
4	Han <i>et al.</i> (2015) [8]	N/A (1/10)10% OF	(10/15) 66.7%	(5/15) 33.3%	TrJOF: (3/10) 30%
5	Kumar <i>et al.</i> (2015) [9]	(2/10)20% COF (3/10)30% POF	(4/10) 40% (JOF)		0%
6	Titinchi <i>et al.</i> (2016) [10]	(61/61) 100%	N/A	N/A	(1/22) 4.5% TrJOF: (4/9) 44%
7	Liu Y <i>et al.</i> (2017) [11]	(29/50) 58%	(12/50) 24%	(9/50) 18%	PsJOF: (2/8) 25%
8	Liu JJ <i>et al.</i> (2017) [12]	(9/13) 69.2%	N/A	(4/13) 30.8%	PsJOF: (2/4) 50% OF: (1/13) 7.6%

*OF: Ossifying fibroma, COF: Central-Ossifying Fibroma, POF: Peripheral Ossifying Fibroma, JOF: Juvenile Ossifying Fibroma, TrJOF: Trabecular Juvenile Ossifying Fibroma, PsJOF: Psammomatoid Juvenile Ossifying Fibroma.

Methodological quality of the study

Authors assessed the methodological quality of all the studies using critical appraisal for treatment study available at www.cebm.net. since it is a valid measure of the methodological quality for treatment study and it provides a comprehensive measure. Because all included studies are case series which did not have control group, also because all the studies are retrospective study, they could not adjust exposure (treated equally for each sample and blinding cannot be applied) during the study. For this reason, all the studies had low level of evidence (level 4) based on center of evidence medicine University of Oxford 2011.

Risk assessment of bias

Authors assessed risk of bias using Joanna Briggs Critical Appraisal Tool for Case Series Study. After evaluating risk of bias, we found 2 case series study with possible high risk of bias (Liu Y *et al.* [5] and Liu JJ [12]). This could be cause by unclear methodology, eligibility criteria of study and demographic report of study. However, most of studies included in this review show low risk of bias after assessment.

Outcome measurement and finding

Demographic Characteristic of Sample and Type Ossifying fibroma

After classified based on WHO Classification for Ossifying Fibroma 2017, authors found female more frequent than male with predisposing age of group below 18 years old. This finding in line with previous systematic review conducted by

Macdonald-Jankowski [13] reported that OF affected females more frequently than males with male to female ratio 1: 2.5, compared with our review was 1: 1.2. Another systematic review conducted by Al-Jazeera *et al.* [14] also reported similar, they found female were having more frequent presentation in elder ages, with 28% above 40 years of age while males only having 8% of cases above this age. Group range that predisposing to having OF reported vary in each review, it could be influence by demographic characteristic by each study. The most frequent type of OF was Classical OF, followed with TrJOF and in the last was PsJOF based on our review. Previous systematic review conducted by Charnovic *et al.* [15] which collected study related JOF found that TrJOF was more frequent than PsJOF. They stated TrJOF frequently happen in younger of child.

Analysing recurrence rate based on type of surgery and type of OF

The role type of surgery to decrease recurrence level of OF had been discuss in recent years. Several studies have reported on the type of surgery and the level of recurrence. From 8 studies have been analyzed, radical surgery being promising treatment to decrease level of recurrence after surgery. This finding also similar with systematic review conducted by Charnovic [15], in their series recurrence rate after radical surgery was 1.6% compared with conservative surgery 38.4%. In our series reported similar with different percentage, recurrence after radical treatment was 11.8% compared with conservative treatment was 19.7%. McDonald-Jankowsky *et al.* [13] also reported similar, conservative treatment such as curettage had high occurrence to recur after surgery. Other studies

stated that complete excision of a OF lesion is the treatment of choice and it can be curative then decreased level of recurrence [16]. Type of OF also contributed to recurrence level. After assessing 8 studies, level of recurrence was high in TrJOF subtype with percentage 36.8%, followed with PsJOF 33.3% and OF 10.6%. This finding in line with several studies that report TrJOF as aggressive disease with high recurrence [15,17]. Another factor that may degrading level of recurrence was well defined margin of tumor based on CT imaging. Reported by Charnovic *et al.* [15] and Liu Y *et al.* [11] discrepancy level of recurrence between well-defined margin and ill-defined margin of CT imaging almost 25%. Based on this, tumor with locally aggressive with ill-defined margin on imaging consider more aggressive treatment like radical surgery. Another issue that also questioning was defect occur during growth period. Several studies reported problem of defects that occur during the growth period especially in pediatric patients can be solved by free flap grafting [18–20].

Another approach that may decrease level of recurrence is endoscopic surgery, especially for tumors located in paranasal sinus. In several studies conducted recent years reported succession of endoscopic surgery to decrease recurrence level of OF. Wang *et al.* [3] reported from 31 patient with OF who underwent endoscopic surgery, 4 from them developed recurrence (percentage of recurrence was 13%). All recurrent cases were juvenile type of OF that possibly behave more aggressively. Another factor may contribute was extension of the tumors. All recurrent cases had involving site minimal in two paranasal sinuses, extended to nasal cavity, orbital and anterior cranial fossa. It seems that for cases with advance tumor extension, resection by endoscopic approach alone had limitation for totally remove the mass.

Recurrence time

From 2 studies conducted by Liu Y *et al.* [11] and Han *et al.* [8], reported similar average time of recurrence, it could be happened between 1 years until 5 years after surgery, with 75% will recur in 1 years post-operative. Several previous studies suggested that the aggressive growth and tendency to recur is age-related and is seen more frequently in the younger age groups. However, after analysing correlation between them, Charcanovic [15] reported no correlation was observed between age and recurrence based on statistical significance.

Conclusion

Overall, all variant of OF, Juvenile Ossifying Fibroma, especially TrJOF, show high recurrence percentage comparing other type. The recurrence level could be influenced by treatment management that chosen by physician. Based on this review first-choice management for treating was surgical approach. Types of surgery to choose to depend on the aggressiveness and morbidity of the disease. After analysed

articles included in this study radical surgery was shown as promising approach to lowering level of recurrence than conservative surgery.

Limitation of this study was all included study in the form of retrospective case series study which certainly has low level of evidence. When the authors look for research that correlates with Ossifying Fibroma research that is available in several databases are primary study in the form of case reports or case series. With this it can be concluded that there is a knowledge gap in analyzing the OF cases. It might be affected by the low prevalence of the disease. To answer other factors that can influence or prognostic factors that correlate with the level of postoperative recurrence, appropriate studies are needed, such as cohort to assess the influential prognostic factors.

Conflicts of interests: The authors declare that they have no conflicts of interest in relation to the publication of this article.

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